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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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09/395,409

09/14/1999

CHARLES CANTOR

17120-006002/2403D

6005

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EXAMINER

CALAMITA, HEATHER

ART UNIT

PAPER NUMBER

1637

MAIL DATE

DELIVERY MODE

04/17/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Advisory Action</b> <b>Before the Filing of an Appeal Brief</b>	Application No.	Applicant(s)	
	09/395,409	CANTOR ET AL.	
	Examiner	Art Unit	
	Heather G. Calamita, Ph.D.	1637	

**--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

THE REPLY FILED 28 March 2007 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.  
b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on \_\_\_\_\_. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

#### AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because  
(a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);  
(b) ☐ They raise the issue of new matter (see NOTE below);  
(c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or  
(d) ☐ They present additional claims without canceling a corresponding number of finally-rejected claims.

NOTE: \_\_\_\_\_. (See 37 CFR 1.116 and 41.33(a)).

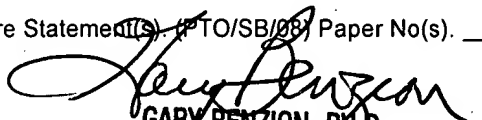
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).  
5. ☐ Applicant's reply has overcome the following rejection(s): \_\_\_\_\_.  
6. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).  
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.  
The status of the claim(s) is (or will be) as follows:  
Claim(s) allowed: \_\_\_\_\_.  
Claim(s) objected to: \_\_\_\_\_.  
Claim(s) rejected: 1-49, 51-54, 58-60, 63-76, 86, 88-124 and 127-147.  
Claim(s) withdrawn from consideration: \_\_\_\_\_.

#### AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).  
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing of a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).  
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

#### REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because:  
See Continuation Sheet.  
12. ☐ Note the attached Information Disclosure Statement(s) PTO/SB/08 Paper No(s). \_\_\_\_\_.  
13. ☐ Other: \_\_\_\_\_.

  
**GARY BENZION, PH.D.**  
**SUPERVISORY PATENT EXAMINER**  
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Continuation of 11. does NOT place the application in condition for allowance because: Applicants' arguments have been fully considered but they are not persuasive. Applicants argue the instant claims are drawn to determining the sequence of a target nucleic acid by identifying hybridized probes in the array by determining the molecular weights of hybridized nucleic acids in the target array. Applicants argue the instant claims do not rely on using mass labels for sequencing as taught by Koster. Applicants argue that it is irrelevant that Koster teaches using mass labels for sequencing and Cantor teaches probe hybridization and sequence determination. These arguments are not persuasive because as outlined in the rejection it would be obvious to use the concept of mass labels as taught by Koster with the concept of sequence determination by hybridization of nucleic acids to an array as described by Cantor. Applicants argue Koster does not teach or suggest identifying hybridized probes in an array based on molecular weight of the hybridized nucleic acids. Again Koster is relied on to teach the concept of using mass labels for identifying nucleic acid sequences. Applicants argue there is no suggestion or teaching in Cantor of identifying hybridized probes in an array by determining the molecular weights of the hybridized nucleic acids in the target array. This is not persuasive because Cantor does teach identifying nucleic acids hybridized to an array with a label. Cantor does not teach identifying the label is a mass label, however, Cantor is not relied on for this teaching because Koster teaches the concept of using a mass label for identification of nucleic acids. With respect to the arguments pertaining to claims 124, 129 and 144-147, these arguments similarly attack the references of Koster and Cantor in a piecemeal manner and are not persuasive because the rejection clearly outlines what elements of the claim are taught by Koster and what elements of the claim are taught by Cantor as well as providing motivation to combine the two teachings. With regard to claim 28, Applicants arguments are moot with the above clarification of the combination of the teachings of Cantor and Koster. With regard to the 103 (a) rejections of claims 71 and 72, Applicants argue the combination of the teachings of Köster and Cantor does not result in the instantly claimed methods. Köster's and Cantor's teachings have been addressed above. Applicant argues Sanghvi does not teach or suggest the use of dimethoxytrityl or a derivative thereof as a selectively releasable bond by which to attach a probe to a solid support. Sanghvi does not teach or suggest using mass spectrometry, or using mass spectrometry for sequencing nucleic acids, or hybridizing a set of nucleic acid fragments containing a sequence that corresponds to a sequence of the target nucleic acid to an array of nucleic acid probes to form a target array of nucleic acids. Sanghvi does not teach or suggest identifying hybridized probes by molecular weight, whereby the sequence of the target nucleic acid is determined. In response to Applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Sanghvi is relied upon for teaching the selectively releasable bond is 4,4'-dimethoxytrityl or a derivative thereof (see example 81 and col. 58 lines 3-32). Further as discussed above, Köster teaches determining molecular weights of nucleic acids in the target array to identify hybridized probes and subsequently determining the sequence of the target nucleic acid (see the abstract). Köster states, "The invention utilizes the Sanger sequencing strategy and assembles the sequence information by analysis of the nested fragments obtained base-specific chain-termination via their different molecular masses using mass spectrometry, as for example, MALDI or ES mass spectrometry. A further increase in throughput can be obtained by introducing mass-modifications in the oligonucleotide primer the chain-terminating nucleoside triphosphates and/or in the chain-elongating nucleoside triphosphates, as well as using integrated tag sequences which allow multiplexing by hybridization of tag specific probes with mass-differentiated molecular weights (see p. 9 lines 23-31). The combination of Köster and Sanghvi meet the limitations recited in claims 71 and 72.